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Review article

Brucellosis: Why is it eradicated from domestic livestock in the United States but not in the Nile River Basin countries?

Ahmed F. Hikal[1], **Gamal Wareth**[2,3] **and Ashraf Khan**[1*]

[1] Division of Microbiology, National Center for Toxicological Research (NCTR), Food and Drug Administration (FDA), Jefferson, Arkansas, USA
[2] Institute of Bacterial Infections and Zoonoses, Fredrich-Loeffler-Institut, 07743 Jena, Germany
[3] Institute of Infectious Diseases and Infection Control, Jena University Hospital, 07747, Jena, Germany

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***Corresponding author:**
Ashraf Khan
ashraf.khan@fda.hhs.gov

Abstract
Brucellosis is one of the most highly infectious zoonotic diseases worldwide and has substantial health and economic impact. Strenuous efforts are essential to combat and prevent this disease from the one-health perspective. Brucellosis is successfully eradicated from domestic animals in the United States, but control strategies continue to eradicate it from wildlife in the Greater Yellowstone Area (GYA). Brucellosis in the Nile River Basin countries (Egypt, Sudan, Ethiopia, and Tanzania) is highly prevalent and endemic. There are several factors behind the failure of eradication of *Brucella* in these countries. The lack of cooperation between policymakers, health officials, veterinary sectors, and farmers is the key reason that impedes the control and prevention strategies in brucellosis-endemic countries. This review will focus on the epidemiology, prevention, and control strategies of *Brucella abortus* and *Brucella melitensis* in the United States and the Nile Basin countries (Egypt, Sudan, Ethiopia, and Tanzania).

Keywords: Brucellosis, USA, Nile Basin, Eradication, Livestock

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Background

Brucella was first isolated by Sir David Bruce in 1887 from soldiers who died from Malta fever, and the organism was first named *Micrococcus melitensis* but was renamed later to *Brucella* (Tan and Davis, 2011). Brucellosis is among the most common zoonotic diseases worldwide that cause substantial economic losses in livestock. The main disease manifestations of brucellosis in animals are abortion and placental retention in females, whereas it causes orchitis and epididymitis in males (Khan and Zahoor, 2018). Brucellosis in humans is mainly an occupational disease affecting people in close contact with infected animals, such as farmers, veterinarians, slaughterhouse workers, and laboratorians. In humans, brucellosis is mainly a febrile disease that usually progresses to chronicity and persistence (Franco et al., 2007). The disease in humans can lead to abortion, splenic abscess, endocarditis, encephalitis, orchitis, and arthritis (Dagli et al., 2011; Zhong et al., 2013).

The major concern of *Brucella* is that it can be easily transmitted via aerosol and used as a possible biological (B-) weapon (Neubauer, 2010). In the past, *Brucella* used to be merged with the free-living *Ochrobactrum*; however, after the consensus agreement among researchers to reclassify them into separate genera, *Brucella* ended up containing thirteen species, including the most recently discovered *Brucella nosferati* (Roop et al., 2021; Hernández-Mora et al., 2023; Moreno et al., 2023); among these, *B. melitensis, B. abortus, B. suis* (except bv 2), and infrequently, *B. canis*, can infect humans. Interestingly, *Brucella* species that infect wild animals, such as *B. ceti, B. neotomae*, and *B. inopinata*, have been isolated from humans with unknown modes of transmission (Roop et al., 2021). *Brucella* is transmitted from animals to humans through direct contact with animal secretions, aborted materials, or by consumption of contaminated unpasteurized dairy products (Wareth et al., 2014b). This review focuses on the epidemiology and control measures of brucellosis in the United States and the Nile Basin countries (Egypt, Sudan, Ethiopia, and Tanzania).

Brucellosis in the United States

B. abortus is the main cause of brucellosis and infects various domestic and wild animals, such as cattle, buffaloes, camels, horses, bison, and elk. The Federal-State Cooperative Brucellosis Eradication program in the United States started in 1934, when brucellosis was highly prevalent, with antigen reactor rates of 11.5% in the tested cattle (Ragan et al., 2002). In 1965, the number of infected cattle with *Brucella* was around 150,000 cases, then declined dramatically until it reached zero infected cattle in 2000 (Ragan et al., 2002). Why was the brucellosis eradication program successful? Implementing very effective surveillance and preventive strategies were the main factors behind the success of eradicating *B. abortus* in the United States. The brucellosis eradication program started with herd testing as an initial step to identify infected cattle. For example, in Vermont, testing for brucellosis started in 1934 and identified approximately 23,000 infected cattle by 1945; all the reactor cattle were culled (Wise, 1980). To ensure that there were no undetected infected animals, further testing was performed every 30-180 days and continued until there were no reactors (Ragan et al., 2002).

Vaccination was another important element that reinforced the brucellosis eradication program. The live attenuated *B. abortus* strain 19 vaccine has been extensively used to vaccinate female calves (4 months- 1 year of age) since the beginning of the eradication program (USDA, 2003). Because the strain 19 vaccine has some disadvantages, such as induction of abortion in pregnant cows and a persistent titer, which made it difficult to distinguish between the infected and vaccinated animals, it was discontinued in some states and replaced with the *B. abortus* strain RB51 (rough rifampicin-resistant strain) (Dorneles et al., 2015). The RB51 vaccine was approved to be administered to non-pregnant heifers (4-12 months of age) only, as it can also induce abortion in pregnant animals (USDA, 2003; Pinn-Woodcock et al., 2023). As of August 2023, all 50 states reported brucellosis free-class status (USDA, 2023b). However, wildlife has been an impediment to the brucellosis eradication program in the United States.

Brucellosis in The Greater Yellowstone Area (GYA), which encompasses the states of Idaho, Montana, and Wyoming and harbors more than 5,500 bison and 125,000 elk, is still endemic and poses a threat to cattle herds (NAS, 2017). Elk, more than bison, are the main source of potential transmission of brucellosis to cattle, and migration of elk herds outside of Yellowstone National Park, due in part to the introduction of wolves, has contributed to the increase of brucellosis cases in cattle in the GYA area (NAS, 2017). Nonetheless, a recent study indicated that bison could also transmit *B. abortus* to cattle (O'Brien et al., 2017). Therefore, there are ongoing efforts by The U.S. Department of Agriculture (USDA) and its Animal and Plant Health Inspection Service (APHIS), in collaboration with other federal and state agencies, to eradicate brucellosis from the GYA through blood testing and elimination of infected animals (NAS, 2017).

B. melitensis is the main cause of brucellosis in sheep and goats. It also infects humans and causes brucellosis (Malta fever), with an estimated 2.1 million cases globally yearly (Laine et al., 2023). *B. melitensis* was eradicated from sheep and goats in the United States in 1972; since then, it has been considered an exotic disease. Because it is not endemic in the United States, there is no strategic plan or program for controlling *B. melitensis* (USDA, 2023a). The success of the brucellosis eradication program in the United States is reflected in the number of infected humans, where only forty-eight cases of human brucellosis were reported to the Center for Disease Control (CDC) in 2022 (USDA, 2023a).

Preview of brucellosis in the Nile Basin countries

The Nile River is the chief river of Africa. The river drains from Tanzania northward to Egypt around 4,130 miles (with an estimated length of over 6650 km). The Nile Basin is shared by eleven countries: four are among the world's poorest populations, which undergo severe environmental degradation. Seven countries suffer from internal or border conflicts. The estimated total area of the Nile Basin is around 10.3% of the area of Africa. In Nile Basin countries, brucellosis is a major infectious bacterial disease that impacts livestock development, productivity, and human health (Sanogo et al., 2013). Human brucellosis is a highly debilitating infection and clinically may be confused with malaria or typhoid fever. Thus, diagnosing brucellosis in underdeveloped and low-income countries is problematic, where diagnostic services are inadequate or non-existent. The economic burden of brucellosis and its control is more significant in low-income countries. To set up and implement efficient control measures against brucellosis in a geographical area from the perspective of "One-Health", there needs to be sufficient knowledge of the epidemiology of the disease, particularly the species and biotypes involved at the national and regional scale. In addition to its zoonoses significance, brucellosis in livestock is a major concern for the economy and food security in the Nile Basin countries.

In Africa, camel brucellosis, which can be contracted from other infected animals, has not received proper attention from the public health sector or researchers. It is clear that fighting against brucellosis in the Nile Basin is a multidimensional process. Collaboration between veterinarians, physicians, and environmental specialists is required to combat the unique brucellosis situation in the Nile Basin countries. Studies on potential *Brucella* reservoirs, exposed populations, and interspecies transmission pathways are the top priorities to eliminate this disease. Cooperative development between the Nile Basin countries will offer a great opportunity to promote regional integration, realize stability, and improve health.

Brucellosis in Egypt

From a historical perspective, brucellosis has likely been an endemic disease for thousands of years in Egypt. There is evidence of spondylitis and osteoarticular lesions, a common complication of brucellosis in bone remnants from ancient Egyptians (750 BC) (Pappas and Papadimitriou, 2007). Brucellosis was reported in a scientific report for the first time in Egypt in 1939 (Refai, 2003). Since then, the disease has become more prevalent nationwide in farm animals, the environment, and rats, which act as carrier hosts for *Brucella*. Animal brucellosis in Egypt was reviewed in detail by (Refai, 2003) and updated by (Wareth et al., 2014a). Serologic testing is a well-established procedure in Egypt that indirectly proves animal brucellosis in all governorates. Cross-species transmission of *Brucella* is proven to occur. For example, *B. melitensis* clones can cross species barriers and establish a permanent reservoir in cattle and buffaloes (Wareth et al., 2014a). Cultivation and biotyping of *Brucella* isolates are unavailable for all governorates due to a lack of resources. *B. abortus* and *B. melitensis* are the predominant isolates in Egypt. *B. abortus* was isolated from cattle, buffaloes, camels, dogs, and cats (Wareth et al., 2017). Although the main host for *B. melitensis* is sheep and goats, it was also isolated from cattle, buffaloes, camels, dogs, cats, and Nile catfish (Wareth et al., 2014a). *B. suis* bv 1 (Ibrahim, 1996) and bv 2 (Wareth et al., 2023) were isolated from domestic pigs. The inappropriate disposal of infected animal carcasses and viscera resulted in contamination of the environment with *Brucella*. Hot spots of brucellosis are located in the Delta region and upper Egypt around the Nile River (Hegazy et al., 2011a,b). Testing and slaughter (T&S) programs and vaccination are the main programs aiming to control brucellosis in Egypt.

Vaccination has been used on a limited scale in all governorates as another tool to prevent animals from developing the disease; calves are vaccinated with *B. abortus* S19 and adults with BR51 vaccines, whereas *B. melitensis* Rev 1 vaccine is used for small ruminants (Refai, 2002). Despite the money and efforts spent to eradicate brucellosis, it is still endemic among livestock in Egypt; this is due to the lack of awareness among farmers in feeding young calves with contaminated colostrum and milk from infected animals. Also, the unhygienic disposal of aborted materials either in rivers and canals or near feed sources contributed to the persistence of brucellosis. Additionally, inadequate government compensation for positive cases hinders the notification process, and eventually, farmers resort to selling their infected animals illegally. This, of course, is reflected in the rate of infection with the disease in humans.

The prevalence of human brucellosis in Egypt is greatly affected by the prevalence of the disease in animals. Acute febrile illness (AFI) is the common syndrome of human brucellosis reported in many hospitals in Egypt (Afifi et al., 2005). For instance, of 4,490 patients admitted to hospitals in Fayoum governorate who experienced AFI, 321 (7%) were confirmed as brucellosis (during 2002-2003) (Jennings et al., 2007). Although the rate of AFI due to brucellosis has increased in recent decades, no fatalities have been reported in Egypt (Refai, 2002). The infection rate was higher in males than females; all cases were in close contact with animals and had a history of consuming unpasteurized milk products (Jennings et al., 2007). Human brucellosis was reported in 59 women admitted to the Al-Zahraa University Hospital and other hospitals in Cairo with osteoarticular lesions, fever, headache, and abortion (Mohammad et al., 2011). *B. melitensis* bv 1 and *B. abortus* bv 1 strains were recovered from the blood culture of the positive human reactors who had AFI (El-Olemy et al., 1984). *B. melitensis* was also cultured from cerebrospinal fluid (CSF) for the first time in a male suffering from nervous manifestation in Abbassia Fever Hospital in Cairo (Mansour et al., 2009).

In Assiut University Hospital, patients with neurobrucellosis showed highly significant cognitive impairment, such as loss of logical memory, mental control, and visual reproduction (Shehata et al., 2010). Despite the high burden of brucellosis in Egypt and frequent empirical treatment, isolates have remained susceptible to most tested antibiotics. The disease is not only confined to occupational people who have close contact with animals, as people can contract the infection from drinking raw milk and products made from it, which can be contaminated with *Brucella*. The widespread home slaughter, raw milk consumption, and milk products perpetuate human brucellosis. For instance, *B. melitensis* DNA was detected in milk samples from apparently healthy animals (Wareth et al., 2014b). In Egypt, human brucellosis has not received appropriate attention and is often initially diagnosed as typhoid fever and fever of unknown origin (El-Metwally et al., 2011). Carelessness and unhygienic handling of infected animals, either in slaughterhouses or on farms, along with the existence of contaminated milk and meat products in the markets, are still the main factors for maintaining brucellosis among humans in Egypt.

Brucellosis in Sudan

Brucellosis was first reported in the Sudan in 1908 (Osman et al., 2015). Since then, the disease remains one of the major zoonotic diseases among livestock. Studies have provided indirect proof of the disease in cattle, goats, sheep, and camels in different governorates by serological assays (Osman et al., 2015). Infection in cattle, sheep, goats, and camels is widespread throughout Sudan and in human contact (Mokhtar et al., 2007; Omer et al., 2010). *B. abortus* and *B. melitensis* are the predominant species in Sudan. *B. melitensis* bv 3 was isolated from sheep and goats (Musa and Jahans, 1990), while *B. abortus* bv 6 was isolated from cattle. In the Darfur Province of western Sudan, the disease is highly prevalent among cattle in nomadic and semi-nomadic areas (Musa et al., 1990). Mixed grazing of different animal species induces interspecies transmission of brucellosis from classical to non-classical hosts. Infection of camels with brucellosis mainly depends on the *Brucella* species prevalent in other animals sharing their habitat. Infection of camels with *B. abortus* bv 3 was reported in Sudan (Agab et al., 1994). *B. abortus* bv 6 (the most prevalent strain in cattle) was isolated for the first time from camel and the pyometra of a seropositive ewe in Darfur (Western Sudan) and Kassala State (Eastern Sudan), respectively(Musa et al., 2008; Gumaa et al., 2014).

Human brucellosis in Sudan is prevalent nationwide among peoples in nomadic, semi-nomadic, and sedentary populations. Some peculiar habits, such as eating raw meat, raw liver, or other offal with spices and consuming raw milk, are significant epidemiological factors in contracting brucellosis, especially in central Sudan (Mohd, 1989). *B. melitensis* bv 1 and *B. abortus* S19 vaccine strains were isolated from the blood of four seropositive, apparently healthy milkers who work in dairy cattle farms (Osman et al., 2015). In the Melut district, South Sudan, *B. abortus* and *B. melitensis* were serologically detected in cattle, green long-tailed monkeys, sheep, goats, and school children (Sixl et al., 1988). Unfortunately, because Sudan has been at war for the last century, there is no data about the bovine brucellosis surveillance and control program in this country.

Brucellosis in Ethiopia

Ethiopia has the largest livestock population in Africa and is also the 10th largest livestock producer in the world. Ethiopia's agriculture is based on livestock, either for use in farming-related activities or livelihood. Livestock is a source of meat, milk, cheese, butter, manure, and export goods (live animals, hides, and skins). Livestock productivity in Ethiopia is affected by various infectious diseases. Among these diseases, brucellosis has been shown to affect animals and humans (Gumi et al., 2013; Asmare et al., 2014). Brucellosis was first reported in Ethiopia in 1977 in dromedaries (Domenech, 1977). Although cattle are the primary hosts of *B. abortus*, the infection can spread to goats and camels co-grazing with cattle (Megersa et al., 2012). A meta-analysis of *Brucella* seroprevalence in dairy cattle reported that the disease is widely distributed in the country.

The highest prevalence rate was reported among cattle (Haileselassie et al., 2011), small-ruminant (Gumi et al., 2013; Teklue et al., 2013), and camels (Teshome et al., 2003). Camel brucellosis is prevalent in northeastern Ethiopia (Bekele et al., 2013). In rural communities of Ethiopia, cattle and camel brucellosis have significant economic and zoonotic implications due to feeding habits, traditional lifestyles, and disease patterns (Megersa et al., 2011; Bekele et al., 2013). All diagnostic protocols used to study brucellosis in Ethiopia have relied on serological tests.

A recent study showed that the brucellosis seroprevalence rate, which was confirmed by PCR, among domestic animals in Southern and central Ethiopia was 3.95% (Wakjira et al., 2022).

Because of the limited resources, molecular biotyping of the circulating *Brucella* spp. is not commonly conducted in Ethiopia. The first human brucellosis cases in Ethiopia were documented in 1981 (Alemayehu, 1981) as a disease of acute and chronic febrile illness (Seboxa, 1982). The prevalence rate among occupationally exposed people was around 4.8% (16/336) in Addis Ababa (Kassahun et al., 2006), while the prevalence was higher in pastoral communities: Borana (34.9% (30/88)) and in Hamer (29.4% (5/17)), who are constantly exposed to animals and consume raw milk and unprocessed cheese (Regassa et al., 2009). High seropositivity of *Brucella* in all pastoral livestock species tested in Southeast Ethiopia implies human infection risks, meriting the necessity of further studies of the disease in animals and humans (Gumi et al., 2013). In addition to the negligence of policymakers regarding brucellosis, illegal animal trade with neighboring countries has also complicated the efforts to eradicate brucellosis in Ethiopia. More than 95% of cross-border trade in East Africa is through illegal channels. The illegal trade of domestic animals from Ethiopia to Somalia, Djibouti, and Kenya generates revenue of 250-300 million dollars annually (100 times more than the official figure) (Pavanello, 2010). This trade leads to the spreading of animal diseases among the neighboring countries (Pavanello, 2010). However, no studies have been conducted on the relationship between cross-border animal movement and brucellosis occurrences. Intervention programs on brucellosis should be formulated based on a comprehensive understanding of disease occurrence and spatial distribution across the country.

Brucellosis in Tanzania

In Tanzania, brucellosis is prevalent and widely distributed in animals and occupational groups (Swai and Schoonman, 2009, 2010). The disease is associated with abortion in humans and domestic ruminants (Ntirandekura et al., 2020). Investigation of brucellosis among 635 pregnant women in urban settings of Mwanza showed a high level of seropositivity of *B. melitensis* (Nyawale et al., 2023). *B. melitensis* and *B. abortus* were also isolated from patients who suffered from bloodstream infection (Bodenham et al., 2020). Another cross-sectional study that was conducted in Kilosa and Chalinze districts of Tanzania between 2019 and 2020 among healthcare workers and community health workers revealed that the majority of participants were not aware of human brucellosis, and they had inadequate knowledge about the burden and impacts of the disease (Mligo et al., 2022).

In humans, both *B. abortus* and *B. melitensis* were defined as causes of brucellosis with seroprevalences 7.7% and 1.9%, respectively, and mainly associated with assisting in parturition without wearing personal protective equipment (PPE) (Ntirandekura et al., 2021). Using the Rose Bengal Test (RBT) and ELISA, cross-sectional studies on bovine brucellosis in agropastoral areas in Tanzania have shown that brucellosis is highly prevalent in those areas (Swai and Schoonman, 2012; Asakura et al., 2018; Shirima and Kunda, 2016). In the last decades, few studies have been conducted on small ruminants and showed a prevalence between 0% and 2.0% in goats and between 0% and 5.7% in sheep (Assenga et al., 2015; Shirima and Kunda, 2016). Circulation of *Brucella* species, particularly *B. abortus*, and *B. melitensis*, in wildlife species such as lions, wildebeest, impala, zebra, and hyenas was proved by PCR, emphasizing the role of wild animals as reservoirs for infections in domestic animals and humans in Tanzania (Sambu et al., 2021). Despite the high prevalence of brucellosis in Tanzania, the lack of brucellosis awareness among laypeople and health professionals, limited diagnostic tests and resources, as well as the paucity of skilled laboratorians have contributed to the absence of brucellosis control programs (Mengele et al., 2023).

Conclusion

Brucellosis is a major zoonotic disease that causes livestock, milk, and fertility losses. Implementing efficient control strategies has eradicated brucellosis from domestic animals in the United States. In contrast, due to inefficient surveillance and control programs, brucellosis is still endemic in the Nile Basin countries. Several factors contribute to the failure of brucellosis eradication in the Nile River Basin countries: I) Inappropriate disposal of aborted materials in rivers and canals plays an important role in transmitting diseases to healthy animals and humans. This occurs due to a lack of knowledge and awareness toward the burden of brucellosis and the method of its transmission; II) Lack of cooperation between policymakers, health professionals, and stockholders. Health professionals and policymakers should provide medical professionals and veterinary sectors with more information about the epidemiology and risk factors of brucellosis and educate animal owners about the zoonotic risk of this disease. Raising awareness about *Brucella* occurrence in traditional livestock husbandry practice will tremendously impact controlling the disease in animals and humans; III) Insufficient government compensation for infected animals due to economic depression impedes farmers' cooperation with veterinary services. Many farmers resort to illegal selling or hiding sick animals because they do not receive adequate compensation from the government. Moreover, due to a lack of guidance, farmers feed young calves colostrum and milk from infected animals owing to the high prices of substitutes; IV) Public vaccination reluctance. All the available vaccines are live-attenuated, and farmers refuse to introduce strains in their farms to avoid the risk of infection; V) Open borders and uncontrolled animal movements between countries and within each country contribute to spreading and disseminating brucellosis across borders; VI) Lack of proper diagnostics and biotyping methods and tools. A comprehensive knowledge of the epidemiology of brucellosis and standard diagnostic capabilities are prerequisites for valid, accurate diagnosis, surveillance, and control.

Finally, the 'test-and-slaughter' strategy and the pasteurization of milk, which have been implemented successfully in the more economically developed countries, might not be the optimal control tools in most African countries due to scarcity of resources. Control strategies should suit the needs and perceptions of each country. Advanced intersectoral and international collaboration regarding surveillance, diagnosis, control, and medical and veterinary personnel education are essential in brucellosis eradication programs.

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References

Afifi, S., Earhart, K., Azab, M.A., Youssef, F.G., El Sakka, H., Wasfy, M., Mansour, H., El Oun, S., Rakha, M., Mahoney, F., 2005. Hospital-based surveillance for acute febrile illness in Egypt: A focus on community-acquired bloodstream infections. The American Journal of Tropical Medicine and Hygiene 73, 392–399. URL: https://www.ncbi.nlm.nih.gov/pubmed/16103611.

Agab, H., Abbas, B., el Jack Ahmed, H., Maoun, I.E., 1994. First report on the isolation of *Brucella abortus* biovar 3 from camel (*Camelus dromedarius*) in the Sudan. Revue d'elevage et de Medecine Veterinaire des Pays Tropicaux 47, 361–363. URL: https://www.ncbi.nlm.nih.gov/pubmed/7770659.

Alemayehu, E., 1981. Brucellosis: A case report. Ethiopian Medical Journal 19, 21–24.

Asakura, S., Makingi, G., Kazwala, R., Makita, K., 2018. Brucellosis risk in urban and agro-pastoral areas in Tanzania. Ecohealth 15, 41–51. 10.1007/s10393-017-1308-z.

Asmare, K., Krontveit, R.I., Ayelet, G., Sibhat, B., Godfroid, J., Skjerve, E., 2014. Meta-analysis of brucella seroprevalence in dairy cattle of Ethiopia. Tropical Animal Health and Production 46, 1341–1350. 10.1007/s11250-014-0669-3.

Assenga, J.A., Matemba, L.E., Muller, S.K., Malakalinga, J.J., Kazwala, R.R., 2015. Epidemiology of *Brucella* infection in the human, livestock and wildlife interface in the Katavi-Rukwa ecosystem, Tanzania. BMC Veterinary Research 11, 189. 10.1186/s12917-015-0504-8.

Bekele, W.A., Tessema, T.S., Melaku, S.K., 2013. *Camelus dromedarius* brucellosis and its public health associated risks in the Afar National Regional State in Northeastern Ethiopia. Acta Veterinaria Scandinavica 55, 89. 10.1186/1751-0147-55-89.

Bodenham, R.F., Lukambagire, A.S., Ashford, R.T., Buza, J.J., Cash-Goldwasser, S., Crump, J.A., Kazwala, R.R., Maro, V.P., McGiven, J., Mkenda, N., Mmbaga, B.T., Rubach, M.P., Sakasaka, P., Shirima, G.M., Swai, E.S., Thomas, K.M., Whatmore, A.M., Haydon, D.T., Halliday, J.E.B., 2020. Prevalence and speciation of brucellosis in febrile patients from a pastoralist community of Tanzania. Scientific Reports 10, 7081. 10.1038/s41598-020-62849-4.

Dagli, O., Dokur, M., Guzeldag, G., Ozmen, Y., 2011. Acute renal failure due to *Brucella melitensis*. Journal of Infection in Developing Countries 5, 893–895. 10.3855/jidc.1442.

Domenech, J., 1977. Serological survey on camel brucellosis in Ethiopia. Revue d'élevage et de Médecine Vétérinaire des Pays Tropicaux 30, 141. URL: http://revues.cirad.fr/index.php/REMVT/article/view/8090, 10.19182/remvt.8090.

Dorneles, E.M.S., Sriranganathan, N., Lage, A.P., 2015. Recent advances in *Brucella abortus* vaccines. Veterinary Research 46, 76. 10.1186/s13567-015-0199-7.

El-Metwally, M.T., Elwan, M.A., El-Bahnasawy, M.M., Khalil, H.H.M., Sabah, A.A.A., Morsy, A.T.A., 2011. Zoonotic brucellosis: An underestimated or misdiagnosed disease in Egypt. Journal of the Egyptian Society of Parasitology 41, 35–46. URL: https://www.ncbi.nlm.nih.gov/pubmed/21634240.

El-Olemy, G.M., Atta, A.A., Mahmoud, W.H., Hamzah, E.G., 1984. Brucellosis in man–II. Isolation of the causative organisms with special reference to blood picture and urine constituents. Developments in Biological Standardization 56, 573–578. URL: https://www.ncbi.nlm.nih.gov/pubmed/6489632.

Franco, M.P., Mulder, M., Gilman, R.H., Smits, H.L., 2007. Human brucellosis. The Lancet Infectious Diseases 7, 775–786. 10.1016/S1473-3099(07)70286-4.

Gumaa, M.M., Osman, H.M., Omer, M.M., El Sanousi, E.M., Godfroid, J., Ahmed, A.M., 2014. Seroprevalence of brucellosis in sheep and isolation of *Brucella abortus* biovar 6 in Kassala State, Eastern Sudan. Revue Scientifique et Technique (International Office of Epizootics) 33, 957–965. 10.20506/rst.33.3.2333.

Gumi, B., Firdessa, R., Yamuah, L., Sori, T., Tolosa, T., Aseffa, A., Zinsstag, J., Schelling, E., 2013. Seroprevalence of brucellosis and Q-Fever in Southeast Ethiopian pastoral livestock. Journal of Veterinary Science & Medical Diagnosis 2. 10.4172/2325-9590.1000109.

Haileselassie, M., Kalayou, S., Kyule, M., Asfaha, M., Belihu, K., 2011. Effect of *Brucella* infection on reproduction conditions of female breeding cattle and its public health significance in Western Tigray, northern Ethiopia. Veterinary Medicine International 2011, 354943. 10.4061/2011/354943.

Hegazy, Y.M., Moawad, A., Osman, S., Ridler, A., Guitian, J., 2011a. Ruminant brucellosis in the Kafr El-Sheikh governorate of the Nile Delta, Egypt: Prevalence of a neglected zoonosis. PLoS Neglected Tropical Diseases 5, e944. 10.1371/journal.pntd.0000944.

Hegazy, Y.M., Molina-Flores, B., Shafik, H., Ridler, A.L., Guitian, F.J., 2011b. Ruminant brucellosis in Upper Egypt (2005-2008). Preventive Veterinary Medicine 101, 173–181. 10.1016/j.prevetmed.2011.05.007.

Hernández-Mora, G., Chacón-Díaz, C., Moreira-Soto, A., Barrantes-Granados, O., Suárez-Esquivel, M., Viquez-Ruiz, E., Barquero-Calvo, E., Ruiz-Villalobos, N., Hidalgo-Montealegre, D., González-Barrientos, R., Demeter, E.A., Estrella-Morales, J., Zúñiga-Pereira, A.M., Quesada-Gómez, C., Chaves-Olarte, E., Lomonte, B., Guzmán-Verri, C., Drexler, J.F., Moreno, E., 2023. Virulent *Brucella nosferati* infecting *Desmodus rotundus* has emerging potential due to the broad foraging range of its bat host for humans and wild and domestic animals. mSphere 8, e0006123. 10.1128/msphere.00061-23.

Ibrahim, S., 1996. Studies on swine brucellosis in Egypt. Egyptian Veterinary Medical Association 56, 1–12.

Jennings, G.J., Hajjeh, R.A., Girgis, F.Y., Fadeel, M.A., Maksoud, M.A., Wasfy, M.O., El-Sayed, N., Srikantiah, P., Luby, S.P., Earhart, K., Mahoney, F.J., 2007. Brucellosis as a cause of acute febrile illness in Egypt. Transactions of the Royal Society of Tropical Medicine and Hygiene 101, 707–713. 10.1016/j.trstmh.2007.02.027.

Kassahun, J., Yimer, E., Geyid, A., Abebe, P., Newayeselassie, B., Zewdie, B., Beyene, M., Bekele, A., 2006. Seroprevalence of brucellosis in occupationally exposed people in Addis Ababa, Ethiopia. Ethiopian Medical Journal 44, 245–252. URL: https://www.ncbi.nlm.nih.gov/pubmed/17447390.

Khan, M.Z., Zahoor, M., 2018. An overview of brucellosis in cattle and humans, and its serological and molecular diagnosis in control strategies. Tropical Medicine and Infectious Disease 3. 10.3390/tropicalmed3020065.

Laine, C.G., Johnson, V.E., Scott, H.M., Arenas-Gamboa, A.M., 2023. Global estimate of human brucellosis incidence. Emerging Infectious Diseases 29, 1789–1797. 10.3201/eid2909.230052.

Mansour, A.M., Nakhla, I.I., Sultan, Y.A., Frenck, R.W., 2009. *Brucella meningitis*: First reported case in Egypt. Eastern Mediterranean Health Journal 15, 1040–1044. URL: https://www.ncbi.nlm.nih.gov/pubmed/20187559.

Megersa, B., Biffa, D., Abunna, F., Regassa, A., Godfroid, J., Skjerve, E., 2012. Seroepidemiological study of livestock brucellosis in a pastoral region. Epidemiology and Infection 140, 887–896. 10.1017/S0950268811001178.

Megersa, B., Biffa, D., Niguse, F., Rufael, T., Asmare, K., Skjerve, E., 2011. Cattle brucellosis in traditional livestock husbandry practice in Southern and Eastern Ethiopia, and its zoonotic implication. Acta Veterinaria Scandinavica 53, 24. 10.1186/1751-0147-53-24.

Mengele, I.J., Shirima, G.M., Bronsvoort, B.M., Hernandez-Castro, L.E., Cook, E.A., 2023. Diagnostic challenges of brucellosis in humans and livestock in tanzania: A thematic review. CABI One Health 10.1079/cabionehealth.2023.0001.

Mligo, B.J., Sindato, C., Yapi, R.B., Mathew, C., Mkupasi, E.M., Kazwala, R.R., Karimuribo, E.D., 2022. Knowledge, attitude and practices of frontline health workers in relation to detection of brucellosis in rural settings of Tanzania: A cross-sectional study. One Health Outlook 4, 1. 10.1186/s42522-021-00056-5.

Mohammad, K.I., El Ghazaly, M.M., Zaalouk, T.K.H., Morsy, A.T.A., 2011. Maternal brucellosis and human pregnancy. Journal of the Egyptian Society of Parasitology 41, 485–496. URL: https://www.ncbi.nlm.nih.gov/pubmed/21980785.

Mohd, M.G., 1989. Brucellosis in the Gezira area, Central Sudan. The Journal of Tropical Medicine and Hygiene 92, 86–88. URL: https://www.ncbi.nlm.nih.gov/pubmed/2496237.

Mokhtar, M., Abdelhamed, A., Sarah, M., Abbas, M., 2007. Survey of brucellosis among sheep, goat, camel and cattle in Kassala area, Eastern Sudan. Journal of Animal and Veterinary Advances 6, 635–637.

Moreno, E., Middlebrook, E.A., Altamirano-Silva, P., Al Dahouk, S., Araj, G.F., Arce-Gorvel, V., Arenas-Gamboa, , Ariza, J., *et al.*, 2023. If you're not confused, you're not paying attention: *Ochrobactrum* is not *Brucella*. Journal of Clinical Microbiology 10.1128/jcm.00438-23.

Musa, M., Jahans, K., Fadalla, M., 1990. *Brucella* biovars isolated from nomadic cattle in the Southern Darfur Province of Western Sudan. Journal of Comparative Pathology 102, 49–54. 10.1016/S0021-9975(08)80006-0.

Musa, M.T., Eisa, M.Z.M., El Sanousi, E.M., Abdel Wahab, M.B., Perrett, L., 2008. Brucellosis in camels (*Camelus dromedarius*) in Darfur, Western Sudan. Journal of Comparative Pathology 138, 151–155. 10.1016/j.jcpa.2007.10.005.

Musa, M.T., Jahans, K.L., 1990. The isolation of *Brucella melitensis* biovar 3 from a testicular hygroma of a ram in a nomadic flock of sheep and goats in western Sudan. Journal of Comparative Pathology 103, 467–470. 10.1016/s0021-9975(08)80034-5.

NAS, 2017. Revisiting brucellosis in the Greater Yellowstone area. National Academies of Sciences, Engineering, and Medicine; Division on Earth and Life Studies; Board on Agriculture and Natural Resources; Committee on Revisiting Brucellosis in the Greater Yellowstone Area. National Academies Press (US), Washington (DC). 10.17226/24750.

Neubauer, H., 2010. Brucellosis: New demands in a changing world. Prilozi 31, 209–217. URL: https://www.ncbi.nlm.nih.gov/pubmed/20703193.

Ntirandekura, J.B., Matemba, L.E., Kimera, S.I., Muma, J.B., Karimuribo, E.D., 2020. Association of brucellosis to abortions in humans and domestic ruminants in Kagera ecosystem, Tanzania. Transboundary and Emerging Diseases 10.1111/tbed.13516.

Ntirandekura, J.B., Matemba, L.E., Kimera, S.I., Muma, J.B., Karimuribo, E.D., 2021. Brucellosis and its associated risk factors to humans and domestic ruminants in Kagera Ecosystem, Tanzania. African Health Sciences 21, 523–530. 10.4314/ahs.v21i2.6.

Nyawale, H.A., Simchimba, M., Mlekwa, J., Mujuni, F., Chibwe, E., Shayo, P., Mngumi, E.B., Majid, K.S., Majigo, M., Mshana, S.E., Mirambo, M.M., 2023. High seropositivity of *Brucella melitensis* antibodies among pregnant women attending health care facilities in Mwanza, Tanzania: A cross-sectional study. Journal of Pregnancy 2023, 2797441. 10.1155/2023/2797441.

O'Brien, M.P., Beja-Pereira, A., Anderson, N., Ceballos, R.M., Edwards, W.H., Harris, B., Wallen, R.L., Costa, V., 2017. Brucellosis transmission between wildlife and livestock in the Greater Yellowstone Ecosystem: Inferences from DNA genotyping. Journal of Wildlife Diseases 53, 339–343. 10.7589/2015-12-329.

Omer, M.M., Musa, M.T., Bakhiet, M.R., Perrett, L., 2010. Brucellosis in camels, cattle and humans: Associations and evaluation of serological tests used for diagnosis of the disease in certain nomadic localities in Sudan. Revue Scientifique et Technique (International Office of Epizootics) 29, 663–669. 10.20506/rst.29.3.2003.

Osman, A.E.F., Hassan, A.N., Ali, A.E., Abdoel, T.H., Smits, H.L., 2015. *Brucella melitensis* biovar 1 and *Brucella abortus* s19 vaccine strain infections in milkers working at cattle farms in the Khartoum Area, Sudan. Plos One 10, e0123374. 10.1371/journal.pone.0123374.

Pappas, G., Papadimitriou, P., 2007. Challenges in *Brucella* bacteraemia. International Journal of Antimicrobial Agents 30 Suppl 1, S29–31. 10.1016/j.ijantimicag.2007.06.011.

Pavanello, S., 2010. Working across borders - Harnessing the potential of cross-border activities to improve livelihood security in the Horn of Africa drylands. Overseas Development Institute, London, UK. URL: https://cdn.odi.org/media/documents/6113.pdf.

Pinn-Woodcock, T., Frye, E., Guarino, C., Franklin-Guild, R., Newman, A.P., Bennett, J., Goodrich, E.L., 2023. A One-Health review on brucellosis in the United States. Journal of the American Veterinary Medical Association 261, 451–462. 10.2460/javma.23.01.0033.

Ragan, V.E., Animal, Service, P.H.I., 2002. The Animal and Plant Health Inspection Service (APHIS) brucellosis eradication program in the United States. Veterinary Microbiology 90, 11–18. 10.1016/s0378-1135(02)00240-7.

Refai, M., 2002. Incidence and control of brucellosis in the Near East region. Veterinary Microbiology 90, 81–110. 10.1016/S0378-1135(02)00248-1.

Refai, M., 2003. Brucellosis in animals and man in egypt. Egyptian Journal of Veterinary Sciences 37, 1–31.

Regassa, G., Mekonnen, D., Yamuah, L., Tilahun, H., Guta, T., Gebreyohannes, A., Aseffa, A., Abdoel, T., Smits, H., 2009. Human brucellosis in traditional pastoral communities in ethiopia. International Journal of Tropical Medicine 4, 59–64. URL: https://medwelljournals.com/abstract/?doi=ijtmed.2009.59.64.

Roop, R.M., Barton, I.S., Hopersberger, D., Martin, D.W., 2021. Uncovering the hidden credentials of *Brucella* virulence. Microbiology and Molecular Biology Reviews 85. 10.1128/MMBR.00021-19.

Sambu, R.M., Mathew, C., Nonga, H.E., Lukambagire, A.S., Yapi, R.B., Akoko, J., Fokou, G., Keyyu, J.D., Bonfoh, B., Kazwala, R.R., 2021. Circulating *Brucella* species in wild animals of the Serengeti ecosystem, Tanzania. One Health Outlook 3, 15. 10.1186/s42522-021-00047-6.

Sanogo, M., Abatih, E., Thys, E., Fretin, D., Berkvens, D., Saegerman, C., 2013. Importance of identification and typing of *Brucellae* from West African cattle: A review. Veterinary Microbiology 164, 202–211. 10.1016/j.vetmic.2013.02.009.

Seboxa, T., 1982. Brucellosis in Ethiopia: Four case reports and a study of data available. Ethiopian Medical Journal 20, 189–192. URL: https://www.ncbi.nlm.nih.gov/pubmed/6890443.

Shehata, G.A., Abdel-Baky, L., Rashed, H., Elamin, H., 2010. Neuropsychiatric evaluation of patients with brucellosis. Journal of Neurovirology 16, 48–55. 10.3109/13550280903586386.

Shirima, G.M., Kunda, J.S., 2016. Prevalence of brucellosis in the human, livestock and wildlife interface areas of Serengeti National Park, Tanzania. The Onderstepoort Journal of Veterinary Research 83, a1032. 10.4102/ojvr.v83i1.1032.

Sixl, W., Reinthaler, F., Sixl-Voigt, B., Withalm, H., Stünzner, D., Schneeweiss, W.D., Rosegger, H., Schuhmann, G., Mascher, F., 1988. Brucellosis in the upper Nile region–Melut district, Sudan (report). Geographia Medica 1, 71–76. URL: https://www.ncbi.nlm.nih.gov/pubmed/3275090.

Swai, E.S., Schoonman, L., 2009. Human brucellosis: Seroprevalence and risk factors related to high risk occupational groups in Tanga Municipality, Tanzania. Zoonoses and Public Health 56, 183–187. 10.1111/j.1863-2378.2008.01175.x.

Swai, E.S., Schoonman, L., 2010. The use of Rose Bengal plate test to asses cattle exposure to *Brucella* infection in traditional and smallholder dairy production systems of Tanga region of Tanzania. Veterinary Medicine International 2010. 10.4061/2010/837950.

Swai, E.S., Schoonman, L., 2012. A survey of zoonotic diseases in trade cattle slaughtered at Tanga city abattoir: A cause of public health concern. Asian Pacific Journal of Tropical Biomedicine 2, 55–60. 10.1016/S2221-1691(11)60190-1.

Tan, S.Y., Davis, C., 2011. David Bruce (1855-1931): Discoverer of brucellosis. Singapore Medical Journal 52, 138–139. URL: https://www.ncbi.nlm.nih.gov/pubmed/21451919.

Teklue, T., Tolosa, T., Tuli, G., Beyene, B., Hailu, B., 2013. Sero-prevalence and risk factors study of brucellosis in small ruminants in Southern Zone of Tigray Region, Northern Ethiopia. Tropical Animal Health and Production 45, 1809–

1815. 10.1007/s11250-013-0439-7.
Teshome, H., Molla, B., Tibbo, M., 2003. A seroprevalence study of camel brucellosis in three camel-rearing regions of Ethiopia. Tropical Animal Health and Production 35, 381–390. URL: https://www.ncbi.nlm.nih.gov/pubmed/14620582, 10.1023/a:1025874310261.
USDA, 2003. Brucellosis Eradication: Uniform Methods and Rules. The United States Department of Agriculture. URL: https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/nvap/NVAP-Reference-Guide/Control-and-Eradication/Brucellosis.
USDA, 2023a. National Brucellosis Eradication Program. The United States Department of Agriculture. URL: https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/cattle-disease-information/national-brucellosis-eradication/brucellosis-eradication-program.
USDA, 2023b. Status of Current Eradication Programs. The United States Department of Agriculture. URL: https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/sa_animal_disease_information/ct_status_of_eradication_programs.
Wakjira, B.S., Jorga, E., Lakew, M., Olani, A., Tadesse, B., Tuli, G., Belaineh, R., Abera, S., Kinfe, G., Gebre, S., 2022. Animal brucellosis: Seropositivity rates, isolation and molecular detection in Southern and Central Ethiopia. Veterinary Medicine 13, 201–211. 10.2147/VMRR.S372455.
Wareth, G., Abdel-Hamid, N.H., Hamdy, M.E.R., Elmonir, W., Beleta, E.I.M., El-Diasty, M., Abdel-Glil, M.Y., Melzer, F., Neubauer, H., 2023. Whole-genome sequencing (WGS) analysis of *Brucella suis* biovar 2 isolated from domestic pigs in Egypt for epidemiological and genetic diversity tracing. Veterinary Microbiology 277. 10.1016/j.vetmic.2022.109637.
Wareth, G., Hikal, A., Refai, M., Melzer, F., Roesler, U., Neubauer, H., 2014a. Animal brucellosis in Egypt. Journal of Infection in Developing Countries 8, 1365–1373. 10.3855/jidc.4872.
Wareth, G., Melzer, F., El-Diasty, M., Schmoock, G., Elbauomy, E., Abdel-Hamid, N., Sayour, A., Neubauer, H., 2017. Isolation of *Brucella abortus* from a dog and a cat confirms their biological role in re-emergence and dissemination of bovine brucellosis on dairy farms. Transboundary and Emerging Diseases 64, e27–e30. 10.1111/tbed.12535.
Wareth, G., Melzer, F., Elschner, M.C., Neubauer, H., Roesler, U., 2014b. Detection of *Brucella melitensis* in bovine milk and milk products from apparently healthy animals in Egypt by real-time PCR. Journal of Infection in Developing Countries 8, 1339–1343. 10.3855/jidc.4847.
Wise, R.I., 1980. Brucellosis in the United-States- Past, present, and future. Jama-Journal of the American Medical Association 244, 2318–2322. URL: https://pubmed.ncbi.nlm.nih.gov/7001058/.
Zhong, Z., Yu, S., Wang, X., Dong, S., Xu, J., Wang, Y., Chen, Z., Ren, Z., Peng, G., 2013. Human brucellosis in the People's Republic of China during 2005-2010. International Journal of Infectious Diseases 17, e289–292. 10.1016/j.ijid.2012.12.030.